REMARKS

In the Office Action of September 26, 2001, Claims 6 - 17 were rejected. No Claims was allowed. In response, Claims 6, 10 and 14 are amended. Reexamination and reconsideration are respectfully requested in view of the following remarks.

Rejection of Claims 6 - 17 under 35 U.S.C. §112, first paragraph

Claims 1 - 5 were rejected under 35 U.S.C. §112, first paragraph on the alleged grounds that the specification does not reasonably provide enablement for compounds of formula I wherein any of 14 named heterocyclic groups are possible for R_5. In response, Claims 6, 10, and 14 are amended to eliminate "$-(CH_2)_n-R_5$" from the definition of R_4 in the compounds of formula I. Accordingly, it is respectfully submitted that the specification provides enablement for the compounds of Claims 6, 10 and 14 as amended, and that the rejection under 35 U.S.C. §112, first paragraph is thereby overcome.

Rejection of Claims 6, 7, 10, 11, 14 and 15 under 35 U.S.C. §102(b) over Kuefner-Muehl et al

Claims 6, 7, 10, 11, 14 and 15 were rejected under 35 U.S.C. §102(b) as anticipated by Kuefner-Muehl et al (DE 3843117). The Examiner alleges that Kuefner-Muehl et al teach the administration of xanthines as adenosine receptor

antagonists to treat aging-related illness such as the neurodegeneration of Alzheimer's disease.

It is respectfully submitted that this rejection is overcome by the amendments of August 28, 2001, which eliminate cycloalkyl from the definition of R_4 in the compounds of formula I, and by the present amendments, which eliminate "-$(CH_2)_n$—R_5" from the definition of R_4 in the compounds of formula I. A compound of formula (I) having R_4 defined as the specific groups in amended Claims 6, 10 and 14 is neither disclosed nor suggested by Kuefner-Muehl et al. Accordingly, it is respectfully submitted that Claims 6, 7, 10, 11, 14 and 15 as amended are not anticipated by, and would not have been obvious over, Kuefner-Muehl et al.

Rejection of Claims 6 - 17 under 35 U.S.C. §102(b) over Miwa et al

Claims 6 - 17 were rejected under 35 U.S.C. §102(b) as anticipated by Miwa et al (JP 09040652 abstract). The Examiner alleges that Miwa et al teach the administration of compounds of instant formula I wherein Z is substituted phenyl for use in the treatment of degenerative disorders.

This rejection is respectfully traversed. Miwa et al teach a process for producing 5-acylamino-6-aminouracyl derivatives that are said to be useful as intermediates for the production of drugs for the treatment of dementia, urinary system diseases and Parkinson's disease. The reference gives

the chemical structure of two xanthine derivatives which fall under formula I of the present claims, where Z is dioxyphenyl. However, the reference provides only the general statement that the 5-acylamino-6-aminouracyl derivatives are useful as intermediates for producing drugs having the various listed uses, and does not provide any specific teaching directed to any method of administration of an effective amount of the compounds of formula I of the present claims for inhibiting neurodegeneration as required by the Claim 6, for treating neurodegenerative disorders, except for Parkinson's disease and attention deficit hyperactivity disorder, as required by Claim 10 or for treating Alzheimer's disease,as required by Claim 14. (In the Amendment of March 31, 2001, the present claims were amended to exclude Parkinson's disease from the set of diseases treated according to the method of the present invention.) Accordingly, it is respectfully submitted that Claims 6 - 17 are not anticipated by and would not have been obvious over Miwa et al.

Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 6 - 17 are in condition for allowance. Favorable reconsideration is respectfully requested.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135. (File No. 506.38266X00).

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

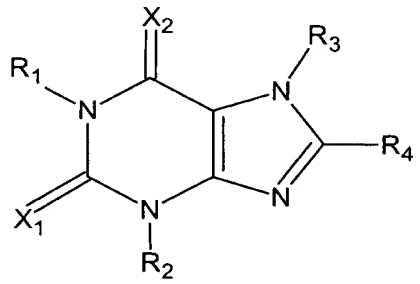
Ralph T. Webb
Registration No. 33,047

RTW/RTW:lcb
Tel.: 703-312-6600
Fax.: 703-312-6666

Marked-up copy to show changes made

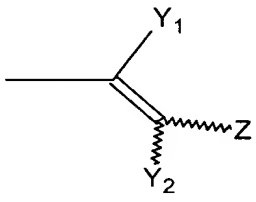
IN THE CLAIMS

6. (twice amended) A method of inhibiting neurodegeneration, which comprises administering an effective dose of a xanthine derivative represented by formula (I):

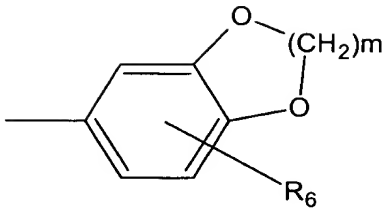


(I)

wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents ~~$-(CH_2)_n-R_5$, wherein R_5 represents a substituted or unsubstituted heterocyclic group selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and n is an integer of 0 to 4, or~~ the following group:



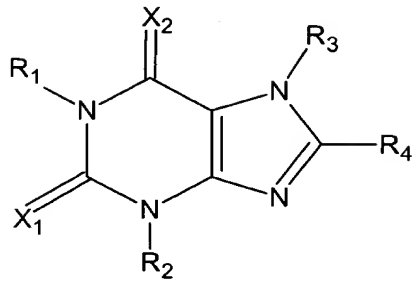
wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:



wherein m is an integer of 1 to 3 and R_6 represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.

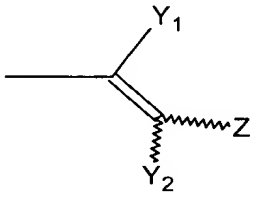
10. (amended) A method of treating neurodegenerative disorders except for Parkinson's disease and attention deficit hyperactivity disorder, which method comprises administering

an effective dose of a xanthine derivative represented by formula (I):

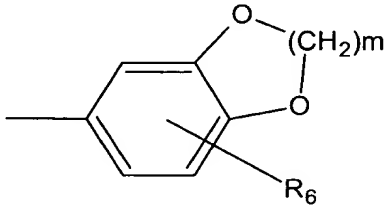


(I)

wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents ~~$-(CH_2)_n-R_5$, wherein R_5 represents a substituted or unsubstituted heterocyclic group selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and n is an integer of 0 to 4, or~~ the following group:



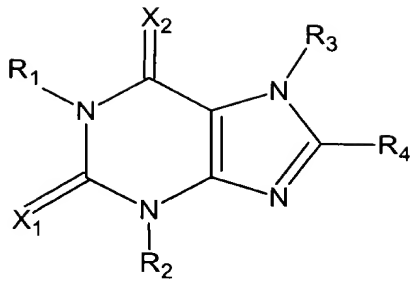
wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:



wherein m is an integer of 1 to 3 and R_6 represents hydrogen,

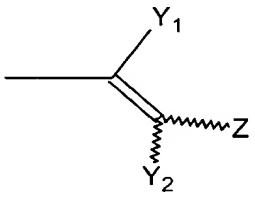
hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.

14. (twice amended) A method of treating Alzheimer's disease, which comprises administering an effective dose of the xanthine derivative represented by formula (I):

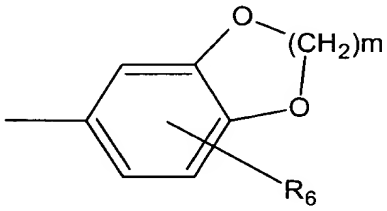


(I)

wherein X_1 and X_2 independently represent O or S, R_1, R_2 and R_3 independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R_4 represents ~~$-(CH_2)_n-R_5$, wherein R_5 represents a substituted or unsubstituted heterocyclic group, selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and n is an integer of 0 to 4, or~~ the following group:



wherein Y_1 and Y_2 independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:



wherein m is an integer of 1 to 3 and R_6 represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected

from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.